

CLAIMS

1. A method of identifying a mammal having or at increased risk of acquiring a proliferative disease, said method comprising the step of determining whether there is a
5 proliferative disease-associated alteration in a *Sal2* nucleic acid of said mammal.

2. The method of claim 1, wherein said method is for identifying a mammal having a proliferative disease.

10 3. The method of claim 1, wherein said method is for identifying a mammal at increased risk of acquiring a proliferative disease.

4. The method of claim 1, wherein said mammal is a human.

15 5. The method of claim 4, wherein said proliferative disease-associated alteration comprises the substitution of a Cys for the Ser at position 73 of SEQ ID NO:1.

6. The method of claim 1, wherein said determining is done by polymerase chain reaction (PCR) amplification, single nucleotide polymorphism (SNP) determination,
20 restriction fragment length polymorphism (RFLP) analysis, hybridization analysis, or mismatch detection analysis.

7. The method of claim 1, wherein said method comprises the steps of:
(i) contacting a first nucleic acid probe which is specific for binding to
25 said human *Sal2* nucleic acid containing said alteration with a nucleic acid from a cell from said mammal under conditions which allow said first nucleic acid probe to anneal to complementary sequences in said cell; and

(ii) detecting duplex formation between said first nucleic acid probe and said complementary sequences.
30

8. The method of claim 7, wherein said first nucleic acid probe is derived from the human *Sal2* nucleic acid containing a proliferative disease-associated alteration.

9. The method of claim 7, further comprising a second nucleic acid probe,
5 wherein said first and second nucleic acid probes are PCR primers, and wherein said human *Sal2* nucleic acid or a fragment thereof is amplified using PCR between steps (i) and (ii).

10. The method of claim 7, wherein said cell is from a physiological sample
10 containing abnormally proliferating tissue.

11. The method of claim 7, wherein said cell is from a physiological sample of normal tissue.

12. The method of claim 7, wherein said alteration comprises the substitution of a Cys for the Ser at position 73 of SEQ ID NO:1.
15

13. A method of identifying a mammal having or at increased risk of acquiring a proliferative disease, said method comprising the step of determining whether there is a proliferative disease-associated alteration in a *Sal2* protein of said mammal.
20

14. The method of claim 13, wherein said method is for identifying a mammal having a proliferative disease.

15. The method of claim 13, wherein said method is for identifying a mammal at increased risk of acquiring a proliferative disease.
25

16. The method of claim 13, wherein said mammal is a human.

17. The method of claim 13, wherein said method comprises the use of an antibody specific for a human *Sal2* protein.
30

18. The method of claim 17, wherein said antibody comprises an antibody specific for a proliferative disease-associated mutant *Sal2* protein.

5 19. A knockout mouse comprising a knockout mutation in a genomic *mSal2* gene.

20. The knockout mouse of claim 19, wherein said mouse further comprises a nucleic acid construct including a mutant *Sal2* gene.

10

21. The knockout mouse of claim 20, wherein said mutant *Sal2* gene is conditionally expressed.

22. The knockout mouse of claim 20, wherein said mutant *Sal2* gene encodes a protein that contains a substitution of a Cys for the Ser at position 73 of SEQ ID NO:1.

15

23. A transgenic mouse whose genome comprises a nucleic acid construct including a *Sal2* nucleic acid, which is operably linked to transcriptional regulatory elements and encodes a *Sal2* protein.

20

24. The transgenic mouse of claim 23, wherein said *Sal2* protein is mutant.

25. The transgenic mouse of claim 23, wherein said transcriptional regulatory elements include a promoter that is a tissue-specific promoter.

25

26. The transgenic mouse of claim 25, wherein said nucleic acid is expressed such that the protein is produced at detectable levels in cells selected from the group consisting of ovarian, bladder, and colon cells.

27. The transgenic mouse of claim 25, wherein said transcriptional regulatory elements include a promoter that is an ovary-specific promoter.

30

28. The transgenic mouse of claim 23, wherein said *Sal2* nucleic acid is a human *Sal2* nucleic acid.

5 29. The transgenic mouse of claim 24, wherein said mouse develops ovarian tumors.

30. The transgenic mouse of claim 29, wherein said ovarian tumors metastasize.

10 31. A cell line derived from cells isolated from said transgenic mouse of claim 23.

32. A method of killing an abnormally proliferating cell, said method comprising the steps of:

- 15 (i) contacting an abnormally proliferating cell with a T-HR mutant specific for a cell carrying a *Sal2* mutation; and
 (ii) allowing said T-HR mutant to lyse said cell.

20 33. The method of claim 32, wherein said T-HR mutant is the TMD-25 T-HR mutant virus.

34. The method of claim 32, wherein said T-HR mutant is administered in a pharmaceutically acceptable carrier.

25 35. The method of claim 32, wherein said abnormally proliferating cell is a mammalian cell.

36. The method of claim 35, wherein said mammalian cell is a human cell.

37. The method of claim 32, wherein said virus is selected from the group consisting of, simian virus 40, human polyoma virus, herpes virus, primate adenoviruses, parvovirus, and papilloma virus.

5 38. A method of identifying a compound which alters cell proliferation, said method comprising:

 a) contacting a first cell with a test compound, and

 b) measuring whether said test compound alters proliferation in said first cell, relative to a second cell not contacted with said test compound, wherein said first
10 and second cells have a proliferative disease-associated alteration in a *Sal2* nucleic acid.

39. The method of claim 38, wherein the ability of said test compound to alter proliferation is measured by measuring the ability of a virus to propagate in said first cell contacted with said test compound, relative to said second cell not contacted with said
15 test compound.

40. The method of claim 39, wherein said virus is a T-HR mutant virus.

41. The method of claim 38, wherein said first and second cells are mammalian
20 cells.

42. The method of claim 38, wherein said first and second cells are in the same mammal or in different mammals.

25 43. The method of claim 42, wherein said mammal is a transgenic mouse.

44. The method of claim 42, wherein said mammal is a knockout mouse comprising a knockout mutation in a genomic *mSal2* gene.

30 45. The method of claim 38, wherein said first and second cells are ovarian cells.

46. A method of identifying a compound which alters cell proliferation, the method comprising:

a) exposing a cell or a cell extract to a test compound, and

b) measuring whether said test compound alters Sal2 levels, relative to

5 Sal2 levels in a cell or cell extract not exposed to said test compound.

47. The method of claim 46, wherein said Sal2 is Sal2 protein.

48. The method of claim 46, wherein said Sal2 is *Sal2* nucleic acid.

10

49. The method of claim 46, wherein said measuring is by measuring Sal2 protein levels.

50. The method of claim 46, wherein said measuring is by measuring *Sal2* nucleic acid levels.

15

51. The method of claim 46, wherein said cell has a proliferative disease-associated alteration in a *Sal2* nucleic acid or said extract is from a cell having a proliferative disease-associated alteration in a *Sal2* nucleic acid.

20

52. The method of claim 46, wherein said exposing is with a cell and said cell is an ovarian cell.

25

30